

Amendments to the Specification:

Please amend the paragraph on page 14, line 31 to page 15, line 5 as follows:

Figure 1. siRNA-mediated inhibition of Livin expression. (a) Predicted secondary structure of pSUPER-Livin-1 and pSUPER-Livin-2 transcripts (**SEQ ID NOS 12 & 13 respectively in order of appearance**). (b) Western blot analysis of Livin protein expression in MeWo melanoma, H1299 lung cancer and HeLa cervical carcinoma cells. Tubulin: detection of α -Tubulin protein expression to monitor equal loading between individual lanes. (c) Inhibition of Livin protein expression in HeLa cells by pSUPER-Livin-1 and pSUPER-Livin-2. Control vector pSUPER-Luc expresses siRNA targeting the *P. pyralis* luciferase gene. (d) Reduction of livin transcripts in HeLa cells by siRNA targeting of livin. Northern blot analysis of poly-A⁺-RNA isolated from HeLa cells transfected with pSUPER-Livin-1, pSUPER-Livin-2, or control transfected HeLa cells, respectively. GAPDH: detection of glyceraldehyde-3-phosphate dehydrogenase transcripts.

Please amend the paragraph on page 15, lines 7-14 as follows:

Figure 2. siRNA against Livin increases Caspase-3 activities in HeLa cells. Livin-positive HeLa and Livin-negative H1299 cells were transfected with either pSUPER-Livin-2 or control vector pSUPER-Luc. DEVD-pNA (**peptide disclosed as SEQ ID NO: 14**) hydrolysis was measured in cytosolic extracts 48 hours post-transfection. Indicated are the Caspase-3 activities of pSUPER-Livin-2-transfected cells relative to control transfectants (pSUPER-Luc), arbitrarily set at 1.0. Values represent the means obtained from at least three independent transfections, error bars indicate the standard deviations. Inclusion of the specific Caspase-3 inhibitor DEVD-fmk (**peptide disclosed as SEQ ID NO: 14**) blocks pSUPER-Livin-2-induced hydrolysis of DEVD-pNA (**peptide disclosed as SEQ ID NO: 14**).

Please amend the paragraph on page 17, line 33 to page 18, line 10 as follows:

Since pSUPER-Livin-2 regularly suppressed endogenous Livin expression more strongly than pSUPER-Livin-1 (Figure 1), the former was chosen for subsequent analyses. It has been

reported that Livin inhibits Caspase-3 activities following ectopic expression from heterologous promoters or in *in vitro* assays. In contrast to these studies, the siRNA approach followed in this study should allow to analyze the effects of endogenous Livin on cellular Caspase-3 activities. As shown in Figure 2, pSUPER-Livin-2 increased Caspase-3-like activities in HeLa cells, indicating that the down-regulation of Livin expression is associated with a release of Caspase-3 from negative regulation by Livin. This conclusion is corroborated by the observation that the Caspase-3 inhibitor DEVD-fmk (peptide disclosed as SEQ ID NO: 14) completely inhibited the increase of DEVD-cleavage (peptide disclosed as SEQ ID NO: 14) following pSUPER-Livin-2 transfection in HeLa cells (Figure 2). In further support for the specificity of the Livin-targeting siRNAs, induction of caspase-3 activities by pSUPER-Livin-2 was observed in Livin-expressing HeLa cells, but not in H1299 cells (Figure 2) which do not express endogenous Livin protein (Figure 1b).

Please amend the paragraph on page 21, lines 25-33 as follows:

Sequence (~~nucleotides 648-668 of SEQ ID NO:11~~):

Livin: ggaagagactttgtccacagt (nucleotides 648-668 of SEQ ID NO:11) GRDFVHS (SEQ ID NO: 15)

LivinMT: ggcagggatttcgtgcattcc (SEQ ID NO: 16) GRDFVHS (SEQ ID NO: 15)

Comparison of livin and livinMT DNA and protein sequences (bold nucleotides represent mutations:

Livin: ggaagagactttgtccacagt (nucleotides 648-668 of SEQ ID NO:11) GRDFVHS (SEQ ID NO: 15)

LivinMT: ggcagggatttcgtgcattcc (SEQ ID NO: 16) GRDFVHS (SEQ ID NO: 15)

Please amend the paragraph on page 22, lines 6-31 as follows:

This could not be achieved with pLivin-alphaMT.

livin-alpha (SEQ ID NO: 10)

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1  gtctgggtggc aggcctgtgc ctatccctgc tgtccccagg gtgggccccg ggggtcagga
61  gctccagaag ggccagctgg gcatattctg agattggcca tcagccccc tttctgctgc
121 aaacctggtc agagccagtg ttccctccat gggacctaaa gacagtgcc aagtgcctgca
181 ccgtggacca cagccgagcc actgggcagc cggatgatgtg cccacgcagg agcgcctgtg
241 acccgcctct ctgggcagcc ctgtcctagg cctggacacc tgcagagcct gggaccacgt
301 ggatgggcag atcctgggga agctgcggcc cctgacagag gaggaagagg aggggggcgc
361 cggggccacc ttgtccaggg ggccctgcctt ccccgccatg ggctctgagg agttgcgtct
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421 ggccctccttc tatgactggc cgctgactgc tgaggtgcc a cccgagctgc tggctgctgc
481 cggcttcttc cacacaggcc atcaggacaa ggtgaggtgc ttcttctgct atgggggcct
541 gcagagctgg aagcgcgggg acgaccctg gacggagcat gccaaagtgg tccccagctg
601 tcagttcctg ctccgggtcaa aaggaagaga ctttgtccac agtgtgcagg agactcactc
661 ccagctgctg ggctcctggg acccggtggg agaaccggaa gacgcagccc ctgtggcccc
721 ctccgtccct gcctctgggt accctgagct gcccacaccc aggagagagg tccagtctga
781 aagtggccag gagccaggag gggtcagtc agcccaggcc cagagggcgt ggtgggttct
841 tgagcccca **ggagccagg** atgtggagg gcagctgcgg cggctgcagg aggagaggac
901 gtgcaaggtg tgccctggacc gcgcctgtgc catcgtctt gtgccgtgcg gccacctggt
961 ctgtgctgag tgtgcccccg gcctgcagct gtgccccatc tgcagagccc cgtccgcag
1021 ccgctgctgc accttctgt cctaggccag gtgccatggc cggccagggt ggctgcagag
1081 tgggctccct gcccctctct gcctgttctg gactgtgttc tgggctgct gaggatggca
1141 gagctggtgt ccatccagca ctgaccagcc ctgattcccc gaccaccgcc caggggtggag
1201 aaggaggccc ttgcttggcg tgggggatgg cttaaactga cctgtttgga tgcttctgaa
1261 tagaaataaa gtgggttttc cctggaggta aaaaaaaaaa aaaaaaaaaa aa

Please amend the paragraph on page 23, lines 1-24 as follows:

livin-beta (SEQ ID NO: 11)

1 ccctgggata ctccccctcc aggggtgtctg gtggcaggcc tgtgcctatc cctgctgtcc
61 ccagggtggg ccccgggggg caggagctcc agaagggcc gctgggcata ttctgagatt
121 ggccatcagc cccatttct gctgcaaacc tggtcagagc cagtgttccc tccatgggac
181 cttaaagacag tgccaagtgc ctgcaccgtg gaccacagcc gagccactgg gcagccggtg
241 atgggtccac gcaggagcgc tgtggacccc gctctctggg cagccctgtc ctaggcctgg
301 acacctgcag agcctgggac cacgtggatg ggcagatcct gggccagctg cggcccctga
361 cagaggagga agaggaggag ggcgcggggg ccaccttgtc cagggggcct gccttccccg
421 gcatgggctc tgaggagtgt cgtctggcct ccttctatga ctggccgctg actgctgagg
481 tgccaccga gctgctggct gctgcccgt tcttccacac aggccatcag gacaaggatga
541 ggtgcttctt ctgctatggg ggctgacaga gctggaagcg cggggacgac ccctggacgg
601 agcatgccaa gtggttcccc agctgtcagt tctgctccg gtcaaaagga agagactttg
661 tccacagtgt gcaggagact cactcccagc tgctgggctc ctgggacccg tgggaagaac
721 cggaagacgc agcccctgtg gcccctccg tccctgcctc tgggtaccct gagctgccc
781 caccaggag agagggtccag tctgaaagtg **cccaggagcc** **aggagccagg** gatgtggagg
841 cgcagctgcg gcggtgcag gaggagagga cgtgcaagg gtgcctggac cgcgcggtgt
901 ccacgtctt tgtgcccgtc ggccacctgg tctgtgctga gtgtgcccc ggctgcagc
961 tgtgccccat ctgcagagcc ccgctccgca gccgcgtgcg caccttctg tccaggcca
1021 ggtgccatgg ccggccagggt gggctgcaga gtgggctccc tgcccctctc tgctgttct
1081 ggactgtgtt ctgggcctgc tgaggatggc agagctggtg tccatccagc actgaccagc
1141 cctgattccc cgaccaccgc ccagggtgga gaaggaggcc cttgcttggc gtgggggatg
1201 gcttaactgt acctgtttgg atgcttctga atagaaataa agtgggtttt ccctggagg

Please amend the paragraph on page 25, lines 25-31 as follows:

To detect caspase-3 protease activities, the ApoAlert Caspase-3 Colorimetric Assay Kit (Clontech, Palo Alto, USA) was utilized. Cytosolic lysates were prepared 48 h following transfection and incubated with 50 μ M p-nitroanilide (pNA) conjugated to the caspase cleavage site Asp-Glu-Val-Asp (DEVD) (**SEQ ID NO: 14**) for 1 h at 37° C. Hydrolyzed pNA was detected using a Multiscan MS colorimeter (ThermoLabsystems, Vantaa, Finland) at 405 nm. For control experiments, 10 μ M of the Caspase-3 inhibitor DEVD-fmk (**peptide disclosed as SEQ ID NO: 14**) (Clontech) was included into the reaction, before addition of the substrate.